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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,955	REHM, BERND	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59,60,64,72-74,76-79,85,88-95,97,100 and 101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59,60,64,72-74,76-79,85,88-95,97,100 and 101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/9/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 12/5/2008 has been entered.

2. Claim amendment filed 12/5/2008 is acknowledged. Claims 59, 60, 64, 72-74, 76-79, 85, 88-95, 97, 100 & 101 are presented and under consideration.

3. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in Germany on 30 August 2002.

4. The Examiner of this application is changed. Please make a note of it.

5. The interview on October 23, 2008 between Applicant's representatives Mr. Gibson, Mr. Mitchard, LC, Examiner Meah M. Y and Nashaat T. Nashed (SPE) is acknowledged. It is noted that during the interview Examiners had suggested to amend the scope of some of the claims to overcome 112 rejections. Examiners also suggested that the prior 103 prior art rejection would be withdrawn subject to prior art search of the *elected invention* and consideration of claims for allowance.

6. Upon further search and review of the current application it was determined that the claims as amended cannot be considered allowable for the following reasons.

7. Applicant's arguments filed with the amendment cited above have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

Any objection or rejection of record not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

8. **New Matter added to claims only** - [New Matter rejection]

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59, 60, 64, 72-74, 76-79, 85, 88-95, 97, 100 & 101 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), **at the time the application was filed**, had possession of the claimed invention. Applicant's addition [new matter] of the claims 59, 60, 64, 72-74, 76-79, 85, 88-95, 97, 100 & 101 are, either directly or in a dependent manner, is not supported by the original disclosure.

Claim 59, for example is drawn to a process for producing polyhydroxy carboxylate particles having surface-bound proteins, the process comprising: at least one gene that codes for a fusion protein, the fusion protein comprising

(a) a polymer synthase from a microorganism of the genera *Ralstonia, Alcaliqenes, Pseudomonas, Aeromonas, or Thiocapsa*, and

(b) at least one biologically active protein selected from an oligopeptide, antibody, abzyme, non-catalytic protein or enzyme.

There is no basis in the instant specification as originally filed, for such fusion constructs. There is also no basis of obtaining gene(s) that codes a **polymer synthase** from a microorganism of the genera *Ralstonia, Alcaliqenes, Pseudomonas, Aeromonas, or Thiocapsa*. These microorganisms have been listed in the specification as possible host cells for culturing - not as a source of 'polymer synthase genes'.

Example 6.2.1 (paragraph 0109), of the instant specification provides a single fusion construct in FLAG-polymer synthase fusion protein: 5'-tatgactagtgattataaagatgatgataaaca-3' and 5'-tatgtttatcatcatctttataatcactagtca-3' (SEQ ID No. 10 and SEQ ID No. 11). Beyond this the specification is silent about the various combination of fusion constructs recite in claim 59.

Applicants are required to cancel the new matter in reply to this office action.
Should Applicants traverse this rejection, Applicants are requested to clearly point the basis of these fusion constructs.

9. ***Written Description***

Claims 59, 60, 64, 72-74, 76-79, 85, 88-95, 97, 100 & 101 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a process for producing polyhydroxy carboxylate particles having surface-bound proteins, the process comprising: at least one gene that codes for a fusion protein, the fusion protein comprising

(a) a polymer synthase from a microorganism of the genera *Ralstonia, Alcaligenes, Pseudomonas, Aeromonas, or Thiocapsa*, and

(b) at least one biologically active protein selected from an oligopeptide, antibody, abzyme, non-catalytic protein or enzyme....., wherein the gene(s) or the encoded protein(s) have defined structure(s).

The specification does not contain any disclosure or description of the structure and function of all gene/protein sequences that are encompassed by the method and capable of producing polyhydroxy carboxylate. The genus of genes/protein that comprise or are used in the process is a large variable genus with no description of the structure. The specification provides a process for producing polyhydroxy carboxylate particles having surface-bound proteins, the process comprising: using a single fusion construct in FLAG-polymer synthase fusion protein: 5'-tatgactagtgattataaagatgatgatgataaaca-3' and 5'-tatgtttatcatcatcatttataatcactagtca-3' (SEQ ID No. 10 and SEQ ID No. 11) of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. The single disclosed species is not representative of the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

10. ***Enablement Rejection***

Claims 59, 60, 64, 72-74, 76-79, 85, 88-95, 97, 100 & 101 in an independent or dependent manner are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for producing polyhydroxy carboxylate particles having surface-bound proteins, the process comprising: using a single fusion construct in FLAG-polymer synthase fusion protein: 5'-tatgactagtgattataaagatgatgatgataaaca-3' and 5'-tatgtttatcatcatcatctttataatcactagtca-3' (SEQ ID No. 10 and SEQ ID No. 11), does not reasonably provide enablement for a process comprising: at least one gene that codes for a fusion protein, the fusion protein comprising -

(a) a polymer synthase from a microorganism of the genera *Ralstonia, Alcaliqenes, Pseudomonas, Aeromonas, or Thiocapsa*, and

(b) at least one biologically active protein selected from an oligopeptide, antibody, abzyme, non-catalytic protein or enzyme....., wherein the gene(s) or the encoded protein(s) have defined structure(s).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of fusion constructs broadly encompassed by the method claims. These fusion constructs includes a combination of a polymer synthase from a microorganism of the genera *Ralstonia, Alcaliqenes, Pseudomonas, Aeromonas, or Thiocapsa and* any oligopeptide, antibody, abzyme, non-catalytic protein or enzyme; Further comprising binding of a biologically active substance to the fusion protein, wherein the biologically active substance is selected from are selected from the group comprising dideoxyinosine, floxuridine, 6-mercaptopurine, doxorubicin, daunorubicin, 1-darubicin, cisplatin, methotrexate, taxol, antibiotics, anticoagulants, germicides, antiarrhythmic agents and active ingredient precursors and derivatives of the listed groups of active ingredients (claim 85), and wherein the biologically active protein is selected from the group comprising insulin, calcitonin, ACTH, glucagon, somatostatin, somatotropin, somatomedin, parathyroid hormone, erythropoietin, hypothalamic release factors,

prolactin, thyroid-stimulating hormone, endorphins, enkephalins, vasopressins, non-naturally occurring opiates, superoxide dismutase, antibodies, interferons, asparaginase, arginase, arginine deaminase, adenosine deaminase, ribonuclease, trypsin, chymotrypsin and pepsin (claim 89), and wherein the coupling reagents preferably being selected from the group comprising bis(2-oxo-3-oxazolydinyl)phosphonic chloride (BOP-Cl), bromotrispyrrolidinophosphonium hexafluorophosphate (PyBroP), benzotriazol-1-yl-oxy-trispyrrolidinophosphonium hexafluorophosphate (PyBOP), n-hydroxysuccinimide biotin, 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), dicyclohexylcarbodiimide, disuccinimidyl carbonate, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC), bis(2-oxo-3-oxazolydinyl)phosphine, diisopropylcarbodiimide (DIPC), 2-(1H-benzotrioxazolyl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU), 2-(5-norbomene-2,3-dicarboxyimido)-1,1,3,3-tetramethyluronium tetrafluoroborate (TNTU), para-nitrophenylchloroformate, and O-(n-succinimidyl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TSTU) (claim 91).

However, in this case the disclosure is limited to a process for producing polyhydroxy carboxylate particles having surface-bound proteins, the process comprising: using a single fusion construct in FLAG-polymer synthase fusion protein: 5'-tatgactagtgattataaagatgatgatgataaaca-3' and 5'-tatgtttatcatcatctttataatcactagtca-3' (SEQ ID No. 10 and SEQ ID No. 11).

While chemical, recombinant and mutagenesis techniques are known, it is not routine in the art to make and use multiple fusion protein constructs further comprising binding biologically active protein(s) to the fusion protein constructs and/or further comprising "chemically modifying the polymer synthase by contacting the polymer synthase with a coupling reagent(s), as encompassed by the instant claims, and the fusion protein constructs can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any fusion protein construct and the result of such modifications is unpredictable. In addition, one skilled in the art would expect such fusion protein constructs or modifications would involve undue experimentation given the limited guidance of a single fusion protein construct.

The specification does not support the broad scope of the claims which encompass preparation of enormous fusion protein constructs and further modification by chemical means because the specification does **not** establish: a rational and predictable and a generalized scheme to uniformly apply the findings of one specific example and extend it include a range of very diversified proteins of claim 89, or further attempt to chemically modify by a host of coupling reagents, as no applicable common procedures are provided for such a method to work effectively and across the board to be successful in enable a process for producing polyhydroxy carboxylate particles having surface-bound proteins using the variety of protein fusion constructs.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of the protein fusion constructs to be employed in the process is unpredictable and the experimentation left to those skilled in the art is improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicant's arguments:

In responding to prior Office Action Applicants argue that without conceding to the rejection, the claims have been amended as discussed during the interview. Based on the present description, it is clear that the invention as claimed is described in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention and that the specification is enabling with regard to the claim scope as now presented. Withdrawal of the written description and lack of enablement rejections is accordingly respectfully requested.

Applicant's arguments are considered but not found to be persuasive because the claims as amended do not reflect subject matter which is described or enabled as explained above. The rejections are therefore maintained.

11. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 89-90 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 89 or 90 recites the limitation "wherein the biologically active protein" in claim 59. There is insufficient antecedent basis for this limitation in the claim.

12. A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant's sequence will not be changed. See MPEP § 608.01(n).

It is suggested that Applicants maintain a proper sequential order where a dependent claim refers to a preceding claims.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached between 8.30 am - 5.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on (571) 272 0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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